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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/873,075	06/01/2001	Allan Svendsen	10038.200-US	4049

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	16

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/873,075	SVENDSEN ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-65* is/are pending in the application.

4a) Of the above claim(s) *49-52 and 54-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-48,53 and 58-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed August 11, 2003 amending the specification to correct clerical informalities, canceling claims 1-32 and adding claims 33-65 has been entered.

Claims 33-65 are pending.

Election/Restriction

During a telephone conversation with Mr. Jason Garbell on January 2, 2003 a provisional election was made with traverse to prosecute the invention of Group I, claims 1, 2, 4 (in part), 7 and 9-13, with election of species of A130. Affirmation of this election must be made by applicant in replying to this Office action. In view of election of species of A130, Group IV, claim 8, which also comprises A130, has been rejoined with Group I.

Applicant did not indicate which of the claims added by the amendment of August 11, 2003 are readable upon the elected species as required by MPEP § 809.02(a).

Currently, claims 33-46 and 58-65 are generic. Claims 47, 48 and 53 correspond to the mutants comprising the elected species of A130.

Claims 49-52 and 54-57 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Terminal Disclaimer

The terminal disclaimer filed on August 11, 2003 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on allowed application 09/857,068 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Objections

Claims 33, 40-42, 45, 46, 58, 59 and 65 are objected to because of the following.

In claims 33 and 58, a comma between "A130" and "Q139" is missing. In claim 40, a comma between "L138" and "T164" is missing.

Claim 45 is objected to because "5° C" should be typed instead of "5°". Appropriate correction is required.

Claims 40, 41, 46 and 59 are objected to because of the following. Claims 40, 41 and 46 depend from claim 33. Claim 33 recites "corresponding to position ... in SEQ ID NO:1", whereas claim 40 recites "corresponding to ... using of SEQ ID NO:1 for numbering" (emphasis added). Claims 41, 42 and 46 recite "corresponding to ... using SEQ ID NO:1 for numbering". Claim 59 is independent and recites "a substitution ... using SEQ ID NO:1 for numbering". It is suggested that applicants maintain consistency throughout the claims and refer to "corresponding to ... in SEQ ID NO: 1" as is the case in independent claims 33 and 58.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47 and 48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 47 and 48 are drawn to a variant cutinase of SEQ ID NO:1 comprising the substitutions corresponding to E6Q+A14P+E47K+R51P+A130+E179Q and E6Q+A14P+N15D+E47K+R51P+A130+E179Q, respectively. While there is support in the specification for the substitutions corresponding to E6Q+A14P+E47K+R51P+A130V+E179Q (page 26, emphasis added), the examiner is unable to locate adequate support for the substitutions corresponding to E6Q+A14P+E47K+R51P+A130+E179Q, i.e. comprising any substitution at position A130. Furthermore, the examiner is unable to locate adequate support for the substitutions corresponding to E6Q+A14P+N15D+E47K+R51P+A130+E179Q, including the substitutions corresponding to E6Q+A14P+N15D+E47K+R51P+A130V+E179Q (emphasis added). Thus there is no indication that mutants comprising the substitutions corresponding to

E6Q+A14P+E47K+R51P+A130+E179Q and E6Q+A14P+N15D+E47K+R51P+A130+E179Q were within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claims 33-48, 53 and 58-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the variants of a parent cutinase of SEQ ID NO:1 that differ from SEQ ID NO:1 by the specific mutations defined in the claims, said variants retaining cutinase activity or hydrolyzing the specific substrates derived from terephthalic acid or having a denaturation temperature which is at least 5° C higher than the "reference" cutinase (E6Q+A14P+E47K+R51P+A130+E179Q mutant of SEQ ID NO:1), does not reasonably provide enablement for a variant of a parent cutinase comprising the same defined mutations wherein the parent cutinase is at least 70% or 80% homologous to SEQ ID NO:1, said variant retaining cutinase activity or hydrolyzing the specific substrates or having a denaturation temperature which is at least 5° higher than the parent or "reference" cutinase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claim 33 is directed to a variant of a parent fungal cutinase, wherein the parent cutinase is at least 70% homologous to SEQ ID NO:1, wherein the variant has above 80% homology to its parent and comprises a modification of at least one defined specific residue. Claim 58 is directed to a variant of a parent fungal cutinase, wherein the parent cutinase is at least 70% homologous to SEQ ID NO:1, wherein the variant differs from the parent cutinase by 1 to 20 substitutions and comprises a modification of at least one defined specific residue. Claim 59 is directed to a variant of a parent fungal cutinase, wherein the parent cutinase is at least 70% homologous to SEQ ID NO:1, wherein the variant has above 80% homology to its parent and a comprises a specific defined substitution. Claims 36 and 61 depend from claims 33 and 59, respectively, and recite the parent cutinase that is at least 80% homologous to SEQ ID NO:1. Claims 37-39 and 62-64 depend from claims 33 and 59, respectively, and recite the variant

cutinase that is at least 85%, 90% or 95% homologous to its parent. Therefore, the claims are drawn to variants of parent cutinases having cutinase activity that have amino acid sequences that are from about 56% to about 80% homologous to SEQ ID NO:1. While all variants must have cutinase activity, claims 43 and 44 which depend from claim 33, limit the hydrolytic activity to the specific substrates. Claim 45 which depends from claim 33, limits a denaturation temperature to at least 5° higher than the parent cutinase at pH 8.5.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of cutinase enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequences of the specific mutants (pages 25-26).

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid

modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. Producing variants as claimed by applicants requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the great number of variants retain the claimed activity.

The specification does not support the broad scope of the claims which encompass variant cutinases with homology to SEQ ID NO:1 ranging from about 56% to about 80% because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting cutinase activity and the regions that are responsible for increasing its thermostability or imparting the specific hydrolyzing patterns; (B) the general tolerance of cutinase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any cutinase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

In addition, with regard to claim 45, the specification is enabling for the specific variants of SEQ ID NO:1 that are more thermostable than the "reference" cutinase (E6Q+A14P+E47K+R51P+A130+E179Q mutant of SEQ ID NO:1). However, the

specification provides no guidance as to how to make a variant that is more thermostable than SEQ ID NO:1 or any parent cutinase that is at least 70% or 80% homologous to SEQ ID NO:1.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a great number of modifications in SEQ ID NO:1.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without necessary guidance, beyond that provided, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Response to Arguments

Applicant's arguments filed August 11, 2003 have been fully considered. The 112, 1st paragraph, written description; 112, 2nd paragraph, and 102(b) rejections are moot in view of the amendment. Applicant's arguments regarding the 112, 1st paragraph, best mode rejection are persuasive (Remarks, pages 10-13). Applicants point out that all disclosed cutinase variants are more thermostable than the reference cutinase (the specification, page 26-27).

With regard to the 112, 1st paragraph, enablement rejection, Applicants argue that limiting the parent cutinase to being at least 70% homologous to the cutinase of

SEQ ID NO:1 overcomes the rejection. This is not persuasive for the reasons discussed above in the rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner

October 28, 2003